09/880,727

09567863

FILE 'HOME' ENTERED AT 14:51:51 ON 05 FEB 2004

=> file reg
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.42	0.42

FILE 'REGISTRY' ENTERED AT 14:53:08 ON 05 FEB 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 4 FEB 2004 HIGHEST RN 646450-50-2
DICTIONARY FILE UPDATES: 4 FEB 2004 HIGHEST RN 646450-50-2

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

*** YOU HAVE NEW MAIL ***

=>
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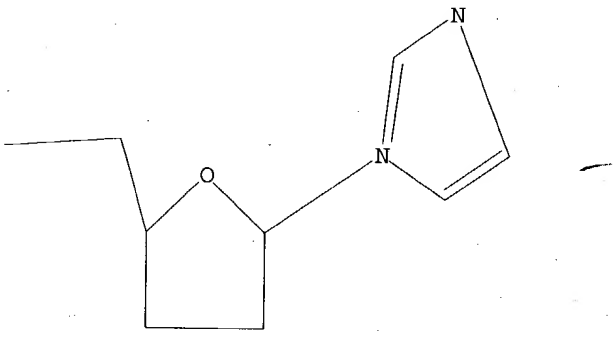
L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1 full
FULL SEARCH INITIATED 14:53:24 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 3077 TO ITERATE

09567863

100.0% PROCESSED 3077 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

L2 0 SEA SSS FUL L1

=>

09567863

FILE 'HOME' ENTERED AT 14:51:51 ON 05 FEB 2004

=> file reg
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.42	0.42

FILE 'REGISTRY' ENTERED AT 14:53:08 ON 05 FEB 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 4 FEB 2004 HIGHEST RN 646450-50-2
DICTIONARY FILE UPDATES: 4 FEB 2004 HIGHEST RN 646450-50-2

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

*** YOU HAVE NEW MAIL ***

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L1 STRUCTURE UPLOADED

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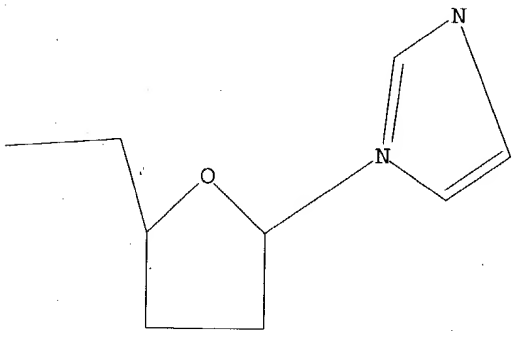
L1 STR



Structure attributes must be viewed using STN Express query preparation.

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FULL SCREEN SEARCH COMPLETED - 3077 TO ITERATE

09567863

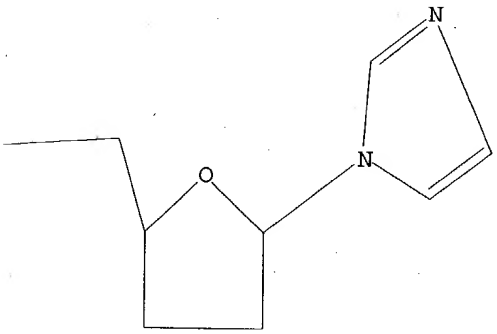
100.0% PROCESSED 3077 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

L2 0 SEA SSS FUL L1

=>
Uploading C:\Program Files\Stnexp\Queries\098807271.str

L3 STRUCTURE UPLOADED

=> d l3
L3 HAS NO ANSWERS
L3 STR



Structure attributes must be viewed using STN Express query preparation.

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FULL SCREEN SEARCH COMPLETED - 3077 TO ITERATE

100.0% PROCESSED 3077 ITERATIONS 1561 ANSWERS
SEARCH TIME: 00.00.01

L4 1561 SEA SSS FUL L3

=> file caplus
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	311.68	312.10

FILE 'CAPLUS' ENTERED AT 14:55:35 ON 05 FEB 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

09567863

FILE COVERS 1907 - 5 Feb 2004 VOL 140 ISS 6
FILE LAST UPDATED: 4 Feb 2004 (20040204/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l4
L5 667 L4

=> s l5 an dlabel?
MISSING OPERATOR L5 AN
The search profile that was entered contains terms or nested terms that are not separated by a logical operator.

=> s l5 and label?
395872 LABEL?
L6 26 L5 AND LABEL?

=> dup rem l6
PROCESSING COMPLETED FOR L6
L7 26 DUP REM L6 (0 DUPLICATES REMOVED)

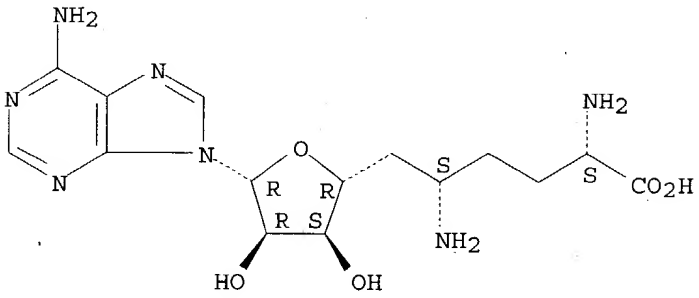
=> d l7 bib abs hitstr 1-26

L7 ANSWER 1 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:122513 CAPLUS
DN 139:97165
TI Photoaffinity **labeling** of the N-methyltransferase domains of cyclosporin synthetase
AU Velkov, Tony; Lawen, Alfons
CS Department of Biochemistry and Molecular Biology, School of Biomedical Sciences, Monash University, Victoria, 3800, Australia
SO Photochemistry and Photobiology (2003), 77(2), 129-137
CODEN: PHCBAP; ISSN: 0031-8655
PB American Society for Photobiology
DT Journal
LA English
AB The multifunctional polypeptide cyclosporin synthetase (Cy-Syn) remains one of the most complex nonribosomal peptide synthetase described. In this study we used a highly specific photoaffinity **labeling** procedure with the natural cofactor S-adenosyl-L-methionine (AdoMet), 14C-isotopically **labeled** at the Sδ Me group to probe the concerted AdoMet-binding interaction of the N-methyltransferase (N-MTase) centers of CySyn. The binding stoichiometry for the enzyme-AdoMet complex was determined to be 1:7, which is in agreement with inferences made from anal. of the complementary DNA sequence of the simA gene encoding the CySyn polypeptide. The photolabeling of the AdoMet-binding sites displayed homotropic neg. cooperativity, characterized by a curvilinear Scatchard plot with upward concavity. Although, the process of N-Me transfer is not a critical event for peptide elongation, the destabilizing homotropic interactions between N-MTase centers that were observed may represent a mechanism whereby the enzyme preserves the proficiency of the substrate-channeling process of cyclosporin peptide assembly over a broad range of cofactor concns. Furthermore, we demonstrated the utility of the photolabeling procedure for tracking the enzyme during purification
IT **58944-73-3**, Sinefungin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(chemical mechanism of S-adenosyl-L-methionine-binding interactions to N-methyltransferase domains of cyclosporin synthetase by photoaffinity **labeling**)
RN 58944-73-3 CAPLUS

09567863

CN D-glycero-α-L-talo-Decofuranuronic acid, 6,9-diamino-1-(6-amino-9H-purin-9-yl)-1,5,6,7,8,9-hexadeoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

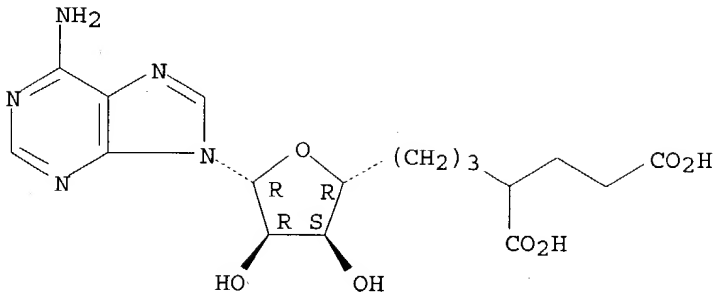


RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:106101 CAPLUS
DN 136:290913
TI A Novel Reaction between Adenosylcobalamin and 2-Methyleneglutarate Catalyzed by Glutamate Mutase
AU Huhta, Marja S.; Ciceri, Daniele; Golding, Bernard T.; Marsh, E. Neil G.
CS Department of Chemistry and Division of Biophysics, University of Michigan, Ann Arbor, MI, 48109-1055, USA
SO Biochemistry (2002), 41(9), 3200-3206
CODEN: BICHAW; ISSN: 0006-2960
PB American Chemical Society
DT Journal
LA English
AB We describe a novel reaction of adenosylcobalamin that occurs when adenosylcobalamin-dependent glutamate mutase is reacted with the substrate analog 2-methyleneglutarate. Although 2-methyleneglutarate is a substrate for the closely related adenosylcobalamin-dependent enzyme 2-methyleneglutarate mutase, it reacts with glutamate mutase to cause time-dependent inhibition of the enzyme. Binding of 2-methyleneglutarate to glutamate mutase initiates homolysis of adenosylcobalamin. However, instead of the adenosyl radical proceeding to abstract a hydrogen from the substrate, which is the next step in all adenosylcobalamin-dependent enzymes, the adenosyl radical undergoes addition to the exo-methylene group to generate a tertiary radical at C-2 of methyleneglutarate. This radical has been characterized by EPR spectroscopy with regiospecifically 13C-**labeled** methyleneglutarates. Irreversible inhibition of the enzyme appears to be a complicated process, and the detailed chemical and kinetic mechanism remains to be elucidated. The kinetics of this process suggest that cob(II)alamin may reduce the enzyme-bound organic radical so that stable adducts between the adenosyl moiety of the coenzyme and 2-methyleneglutarate are formed.
IT **407614-54-4**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(glutamate mutase can catalyze novel reaction between adenosylcobalamin and 2-methyleneglutarate)
RN 407614-54-4 CAPLUS
CN Pentanedioic acid, 2-[3-[(2R,3S,4R,5R)-5-(6-amino-9H-purin-9-yl)tetrahydro-3,4-dihydroxy-2-furanyl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

09567863



RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:98348 CAPLUS
DN 132:146629
TI Autoinducer synthase-modulating compounds for inhibition of bacterial growth
IN Cronan, John E., Jr.; Plapp, Bryce V.; Greenberg, E. Peter; Parsek, Matthew R.
PA The University of Iowa Research Foundation, USA
SO PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000006177	A1	20000210	WO 1999-US17188	19990729
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2003054512	A1	20030320	US 1999-227488	19990106
	CA 2337710	AA	20000210	CA 1999-2337710	19990729
	AU 9955449	A1	20000221	AU 1999-55449	19990729
	EP 1100513	A1	20010523	EP 1999-941978	19990729
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRAI	US 1998-94988P	P	19980731		
	US 1999-227488	A	19990106		
	WO 1999-US17188	W	19990729		

AB A composition for modulating the activity of an autoinducer synthase mol. comprises an effective amount of a compound capable of affecting the binding of an organic or inorg. substrate to the homoserine lactone binding site of the autoinducer synthase, thereby modulating the activity of the autoinducer synthase mol. A method for identifying modulators of the autoinducers synthesis reaction is also provided. Such modulators are useful for controlling bacterial growth and can be used for therapeutic treatment of bacterial infections particularly in immunocompromized subjects, e.g. individuals with cystic fibrosis or HIV infection. They are also useful in treating disease states associated with autoinducer synthesis and biofilm development. To facilitate the study of acyl homoserine lactone (HSL) synthesis by RhlI autoinducer synthase, an in

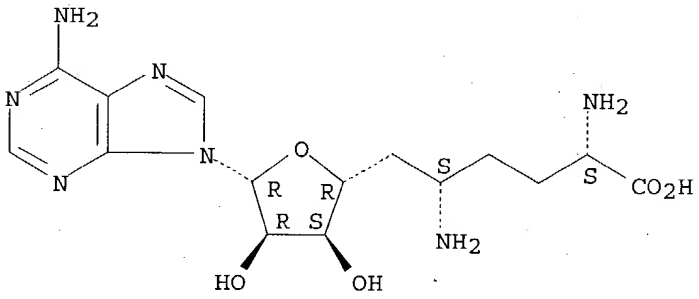
vitro assay using 14C-**labeled** S-adenosine methionine (SAM) was developed. The results verified that RHlI was an autoinducer synthase requiring only butyryl-acyl protein carrier (ACP) and SAM as substrates. The reaction was linear over time and dependent upon the concentration of the enzyme.

IT **58944-73-3**, Sinefungin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(modulation of autoinducer synthase mols. by binding to homoserine lactone binding site for inhibition of bacterial growth)

RN 58944-73-3 CAPLUS

CN D-glycero-α-L-talo-Decofuranuronic acid, 6,9-diamino-1-(6-amino-9H-purin-9-yl)-1,5,6,7,8,9-hexadeoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1998:484268 CAPLUS

DN 129:213362

TI A novel mechanism-based inhibitor (6'-bromo-5',6'-didehydro-6'-deoxy-6'-fluorohomoadenosine) that covalently modifies human placental S-adenosylhomocysteine hydrolase

AU Yuan, Chong-Sheng; Wnuk, Stanislaw F.; Robins, Morris J.; Borchardt, Ronald T.

CS Department of Biochemistry, The University of Kansas, Lawrence, KS, 66047, USA

SO Journal of Biological Chemistry (1998), 273(29), 18191-18197
CODEN: JBCHA3; ISSN: 0021-9258

PB American Society for Biochemistry and Molecular Biology

DT Journal

LA English

AB Most inhibitors of S-adenosylhomocysteine (AdoHcy) hydrolase function as substrates for the "3'-oxidative activity" of the enzyme and convert the enzyme from its active form (NAD+) to its inactive form (NADH) (Liu, S., Wolfe, M. S., and Borchardt, R. T. (1992) Antivir. Res. 19, 247-265). In this study, we describe the effects of a mechanism-based inhibitor, 6'-bromo-5',6'-didehydro-6'-deoxy-6'-fluorohomoadenosine (BDDFHA), which functions as a substrate for the "6'-hydrolytic activity" of the enzyme with subsequent formation of a covalent linkage with the enzyme. Incubation of human placental AdoHcy hydrolase with BDDFHA results in a maximum inactivation of 83% with the remaining enzyme activity exhibiting one-third of the kcat value of the native enzyme. This partial inactivation is concomitant with the release of both Br- and F- ions and the formation of adenine (Ade). The enzyme can be covalently **labeled** with [8-3H]BDDFHA, resulting in a stoichiometry of 2 mol

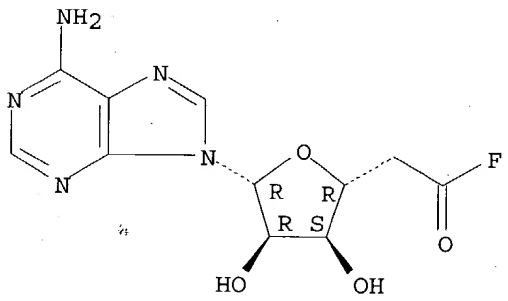
of BDDFHA/mol of the tetrameric enzyme. The 3H-**labeled** enzyme retains its original NAD+/NADH content. Tryptic digestion and subsequent protein sequencing of the [8-3H]BDDFHA-**labeled** enzyme revealed that Arg196 is the residue that is associated with the radiolabeled inhibitor. The partition ratio of the Ade formation (nonlethal event) to covalent acylation (lethal event) is approx. 1:1. From these exptl. results, a possible mechanism by which BDDFHA inactivates AdoHcy hydrolase is proposed: enzyme-mediated water addition at the C-6' position of BDDFHA followed by elimination of Br- ion results in the formation of homoAdo 6'-carboxyl fluoride (HACF). HACF then partitions in two ways: (a) attack by a proximal nucleophile (Arg196) to form an amide bond after expulsion of F- ion (lethal event) or (b) depurination to form Ade and hexose-derived 6-carboxyl fluoride (HDCF), which is further hydrolyzed to hexose-derived 6-carboxylic acid (HDCA) and F- ion (nonlethal event).

IT **212318-28-0**
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(novel mechanism-based inhibitor (6'-bromo-5',6'-didehydro-6'-deoxy-6'-fluorohomoadenosine) that covalently modifies human placental S-adenosylhomocysteine hydrolase)

RN 212318-28-0 CAPLUS

CN β-D-ribo-Hexofuranuronoyl fluoride, 1-(6-amino-9H-purin-9-yl)-1,5-dideoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 5 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1998:450907 CAPLUS

DN 129:175910

TI Discovery of Type II (Covalent) Inactivation of S-Adenosyl-L-homocysteine Hydrolase Involving Its "Hydrolytic Activity": Synthesis and Evaluation of Dihalohomovinyl Nucleoside Analogs Derived from Adenosine

AU Wnuk, Stanislaw F.; Mao, Yue; Yuan, Chong-Sheng; Borchardt, Ronald T.; Andrei, Graciela; Balzarini, Jan; De Clercq, Erik; Robins, Morris J.

CS Department of Chemistry and Biochemistry, Brigham Young University, Provo, UT, 84602-5700, USA

SO Journal of Medicinal Chemistry (1998), 41(16), 3078-3083
CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society

DT Journal

LA English

AB Treatment of the 5'-carboxaldehyde derived by Moffatt oxidation of 6-N-benzoyl-2',3'-O-isopropylideneadenosine with the "(bromofluoromethylene)triphenylphosphorane" reagent and deprotection gave 9-(6-bromo-5,6-dideoxy-6-fluoro-β-D-ribo-hex-5-enofuranosyl)adenine

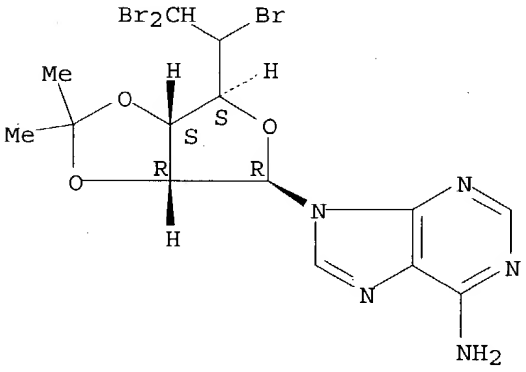
(I). Parallel treatment with a "dibromomethylene Wittig reagent" and deprotection gave 9-(6,6-dibromo-5,6-dideoxy-β-D-ribo-hex-5-enofuranosyl)adenine (II). Bromination-dehydrobromination of the 5'-bromohomovinyl analog and deprotection gave (E)-9-(5,6-dibromo-5,6-dideoxy-β-D-ribo-hex-5-enofuranosyl)adenine (III). Compds. I-III were designed as putative substrates of the "hydrolytic activity" of S-adenosyl-L-homocysteine (AdoHcy) hydrolase. Enzyme-mediated addition of water across the 5,6-double bond could generate electrophilic acyl halide or α-halo ketone species that could undergo nucleophilic attack by proximal groups on the enzyme. Such type II (covalent) mechanism-based inactivation is supported by protein **labeling** with 8-[3H]-I and concomitant release of bromide and fluoride ions. Incubation of AdoHcy hydrolase with II or III resulted in irreversible inactivation and release of bromide ion. In contrast with type I mechanism-based inactivation, reduction of enzyme-bound NAD+ to NADH was not observed Compds. I-III were not inhibitory to a variety of viruses in cell culture, and weak cytotoxicity was observed only for CEM cells.

IT **211507-51-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and antiviral and cytotoxicity of dihalohomovinyl nucleoside analogs as S-adenosyl-L-homocysteine hydrolase inhibitors)

RN 211507-51-6 CAPLUS

CN 9H-Purin-6-amine, 9-[(5ξ)-5,6,6-tribromo-5,6-dideoxy-2,3-O-(1-methylethylidene)-β-D-ribo-hexofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 6 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:450881 CAPLUS
DN 127:188700
TI Transport of S-adenosylmethionine in isolated rat liver mitochondria
AU Horne, Donald W.; Holloway, Rosalind S.; Wagner, Conrad
CS Biochemistry Research Laboratory, Department Veterans Affairs Medical Center, Nashville, TN, 37212, USA
SO Archives of Biochemistry and Biophysics (1997), 343(2), 201-206
CODEN: ABBIA4; ISSN: 0003-9861
PB Academic
DT Journal
LA English
AB Mitochondria do not have the enzyme, methionine adenosyltransferase (ATP: L-methionine S-adenosyltransferase, EC 2.5.1.6), necessary for the biosynthesis of S-adenosylmethionine. Nevertheless, about 30% of total hepatic S-adenosylmethionine resides in the mitochondria and radiolabeled

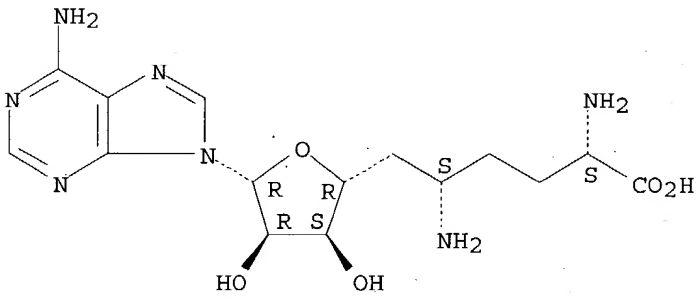
S-adenosylmethionine may be isolated from the mitochondria after administration of radiolabeled methionine. This leads to the hypothesis that a carrier-mediated system is responsible for S-adenosylmethionine transport from the cytosol into the mitochondria. Such a system in isolated rat liver mitochondria has been characterized. Uptake of S-adenosylmethionine consisted of two components. One component was incorporation of the Me group into phospholipids as shown by thin-layer chromatog. The second component represented uptake into the mitochondria since addition of excess unlabeled S-adenosylmethionine resulted in efflux of **labeled** substrate. This counter transport is characteristic of a carrier-mediated transport system. Uptake (corrected for incorporation into phospholipids) was saturable with an apparent Km = 8.9 μM and Vmax = 54.3 pmol·mg protein-1·min-1. Uptake was not inhibited by methionine, adenosine, 5'-methylthioadenosine, carnitine, choline, betaine, quinine, or hemicholinium-3. Uptake was inhibited by sinefungin and by S-adenosylhomocysteine (Ki = 53.4 μM). Uptake of S-adenosylmethionine was not dependent on the elec. potential across the mitochondrial membrane. These results indicate that S-adenosylmethionine is taken up into mitochondria via a specific, carrier-mediated system.

IT **58944-73-3**, Sinefungin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitory effect on uptake of S-adenosylmethionine into isolated rat liver mitochondria)

RN 58944-73-3 CAPLUS

CN D-glycero-α-L-talo-Decofuranuronic acid, 6,9-diamino-1-(6-amino-9H-purin-9-yl)-1,5,6,7,8,9-hexadeoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L7 ANSWER 7 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1997:561438 CAPLUS

DN 127:218756

TI Adhesion of Candida albicans to epithelial cells - effect of nikkomycin

AU Segal, Esther; Gottlieb, S.; Altboum, Z.; Gov, Y.; Berdicevsky, Israela

CS Department of Human Microbiology, Sackler School of Medicine, Tel Aviv University, Tel Aviv-Jaffa, 69978, Israel

SO Mycoses (1997), 40(1/2), 33-39
CODEN: MYCSEU; ISSN: 0933-7407

PB Blackwell

DT Journal

LA English

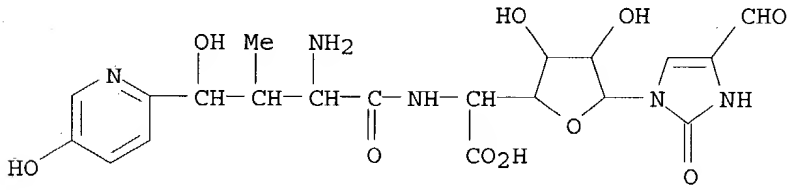
AB This study investigated the effect of the chitin synthetase inhibitors, the nikkomycins (NZ and NZ + NX), on Candida albicans adhesion to buccal epithelial cells (BECs) in vitro. The effect was expressed in reduced chitin synthetase activity and chitin content of fungal cells. In vitro adhesion assays to BECs of Candida exposed to NZ and NZ + NX revealed reduced adhesion values. Light, scanning and transmission electron

microscopy (SEM, TEM) of NZ-treated and untreated micro-organisms showed changed fungal morphol. and reduced adherence of the treated yeasts. SEM of NZ-treated C. albicans **labeled** with gold-conjugated wheat-germ agglutinin (WGA) revealed less **labeling** than in the untreated organisms. A close contact between the fungus and the epithelial cell at a site with intense WGA-gold **labeling** was noted in TEM expts. The data point to the involvement of chitin in the adhesion of C. albicans to epithelial cells.

IT **72864-26-7**, Nikkomycin X
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(effect of nikkomycin on adhesion of Candida albicans to epithelial cells)

RN 72864-26-7 CAPLUS

CN β-D-Allofuranuronic acid, 5-[[(2S,3S,4S)-2-amino-4-hydroxy-4-(5-hydroxy-2-pyridinyl)-3-methyl-1-oxobutyl]amino]-1,5-dideoxy-1-(4-formyl-2,3-dihydro-2-oxo-1H-imidazol-1-yl)- (9CI) (CA INDEX NAME)



L7 ANSWER 8 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1995:680037 CAPLUS

DN 123:107512

TI Effect of 5-azacytidine and singefungin on Streptomyces development

AU Fernandez, Marisol; Soliveri, Juan; Novella, Isabel S.; Yebra, maria J.; Barbes, Covadonga; Sanchez, Jesus

CS Departamento de Biologia Functional, Universidad de Oviedo, Oviedo, Spain

SO Gene (1995), 157(1/2), 221-3
CODEN: GENED6; ISSN: 0378-1119

PB Elsevier

DT Journal

LA English

AB The effect of two DNA-methyltransferase inhibitors, 5-azacytidine (5azaC) and singefungin (Sf), on the development of Streptomyces antibioticus ETH7451 (Sa) was studied. Pulse **labeling** expts. and SDS-PAGE anal. of proteins from cells grown in sporulation synthetic medium showed that both inhibitors affect a limited number of systems. Synthesis of the antibiotic rhodomycin was increased in the presence of 5azaC. 5AzaC also stimulated the production of actinorhodin in cultures of S. coelicolor A3(2) grown in minimal medium. The analog did not affect the expression of whiB and whiG, two sporulation genes from S. coelicolor A3(2) whose homologues are present in Sa. Overall results indicated that 5azaC and Sf affect specific events associated with differentiation and secondary metabolism in Streptomyces.

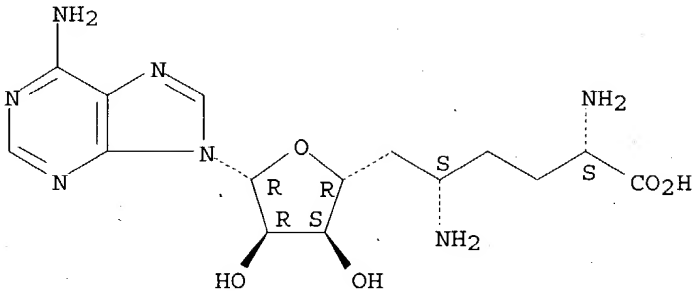
IT **58944-73-3**, Sinefungin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(5-azacytidine and singefungin affect specific events associated with differentiation and secondary metabolism in Streptomyces antibioticus and S. coelicolor A3 development)

RN 58944-73-3 CAPLUS

CN D-glycero-α-L-talo-Decofuranuronic acid, 6,9-diamino-1-(6-amino-9H-purin-9-yl)-1,5,6,7,8,9-hexadeoxy- (9CI) (CA INDEX NAME)

09567863

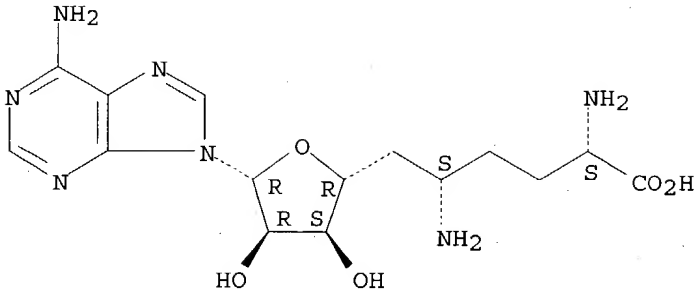
Absolute stereochemistry. Rotation (+).



L7 ANSWER 9 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:430354 CAPLUS
DN 122:209544
TI Leishmania donovani: Enhanced expression of soluble acid phosphatase in the presence of sinefungin, an antiparasitic agent
AU Moulay, Lamya; Robert-Gero, Malka
CS Institut de Chimie des Substances Naturelles, C.N.R.S., Gif-sur-Yvette, 91198, Fr.
SO Experimental Parasitology (1995), 80(1), 8-14
CODEN: EXPAAA; ISSN: 0014-4894
DT Journal
LA English
AB Sinefungin, an antileishmanial nucleoside, induces morphol. and ultrastructural changes in promastigotes of Leishmania donovani. The most important modifications are the enlargement of the flagellar pocket and the increased activity of the Golgi apparatus Cytoenzymic **labeling** demonstrates an increased activity of the soluble acid phosphatase in the flagellar reservoir of sinefungin-treated cells. The affinity constant remained unchanged. Analyzes by Western blot demonstrate an increased amount of the enzyme in the treated cells. The increased amount was not due to impaired enzyme release, as in the external medium the acid phosphatase was also enhanced but to a lesser extent. Under identical conditions the membrane-bound acid phosphatase was not modified. These results indicate that the enlargement of the flagellar pocket is the consequence of the accumulation of acid phosphatase and other Golgi-mediated enzymes provoking unbalanced cytoplasmic exchange. Sinefungin has the same effects on Leishmania tropica promastigotes. However, these effects are not specific to sinefungin. Another mol., taxol, also induced cell rounding accompanied by increased acid phosphatase activity. Under conditions where cell rounding is not observed, in stationary phase or with compds. which stopped proliferation without shape change, no increase in the amount of acid phosphatase could be observed These results clearly demonstrate a correlation between morphol., ultrastructural changes and the stimulated expression of acid phosphatase.
IT **58944-73-3**, Sinefungin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(soluble acid phosphatase enhanced expression by Leishmania donovani induced by sinefungin and cell-rounding drugs)
RN 58944-73-3 CAPLUS
CN D-glycero-α-L-talo-Decofuranuronic acid, 6,9-diamino-1-(6-amino-9H-purin-9-yl)-1,5,6,7,8,9-hexadeoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

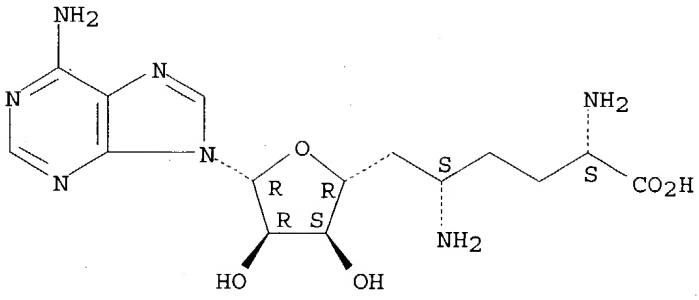
09567863



L7 ANSWER 10 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:477171 CAPLUS
DN 121:77171
TI Photolabeling of the EcoP15 DNA methyltransferase with S-adenosyl-L-methionine
AU Ahmad, Ishtiyaque; Rao, Desirazu N.
CS Department of Biochemistry, Indian Institute of Science, Bangalore, 560 012, India
SO Gene (1994), 142(1), 67-71
CODEN: GENED6; ISSN: 0378-1119
DT Journal
LA English
AB Radioactivity from S-adenosyl-L-[methyl-3H]methionine ([methyl-3H]AdoMet) was bound to the EcoP15 DNA methyltransferase (M·EcoP15) following short-wave UV irradiation The **labeled** protein was subjected to polyacrylamide-gel electrophoresis in the presence of sodium dodecyl sulfate (SDS-PAGE), and detected by fluorog. and autoradiog. **Labeling** was found to be dependent on the concentration of AdoMet and time of UV irradiation The photolabeling by [methyl-3H]AdoMet was specific and blocked by S-adenosyl-L-homocysteine (AdoHcy) and sinefungin which are known to function as competitive inhibitors. Limited digestion of the M·EcoP15-AdoMet adduct by Staphylococcus aureus protease V8 generated three peptides of approx. 50, 32 and 30kDa. Interestingly, only the 30-kDa peptide fragment contained radioactivity, as detected by SDS-PAGE, followed by fluorog. and autoradiog. Further, sequencing of a few amino acids at the N-terminus of these peptides showed that the 30-kDa fragment was the N-terminal portion of M·EcoP15. These results suggest that photolabeling is at the AdoMet-binding site and that the N-terminal half of M·EcoP15 may be involved in substrate binding.
IT **58944-73-3**, Sinefungin
RL: BIOL (Biological study)
(EcoP15 DNA methyltransferase photolabeling with S-adenosyl-L-methionine following short-wave UV irradiation blocked by, binding site in relation to)
RN 58944-73-3 CAPLUS
CN D-glycero-α-L-talo-Decofuranuronic acid, 6,9-diamino-1-(6-amino-9H-purin-9-yl)-1,5,6,7,8,9-hexadeoxy- (9CI) (CA INDEX NAME)

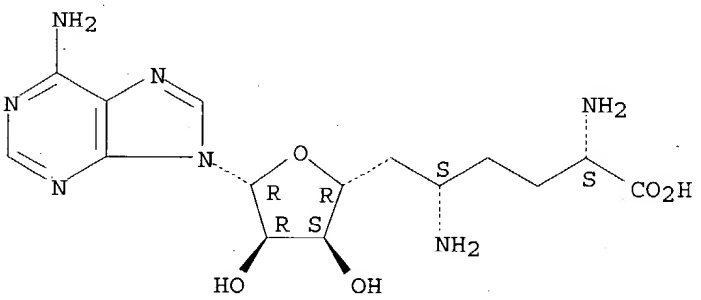
Absolute stereochemistry. Rotation (+).

09567863



L7 ANSWER 11 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:101776 CAPLUS
DN 120:101776
TI Effects of sinefungin on growth and sterol composition of Leishmania promastigotes
AU Haughan, Penny A.; Chance, Michael L.; Goad, L. John
CS Dep. Biochem., Univ. Liverpool, Liverpool, L69 3BX, UK
SO Experimental Parasitology (1993), 77(2), 147-154
CODEN: EXPAAA; ISSN: 0014-4894
DT Journal
LA English
AB The S-adenosylmethionine analog sinefungin was tested in vitro against promastigotes of various strains of Leishmania. The IC50 values for the Leishmania mexicana, Leishmania major, and Leishmania donovani strains used were of the order of 10 ng/mL, but the Leishmania amazonensis strain tested was more resistant to the drug, the IC50 value being 6 μg/mL. Sterol profiles, in which 24-alkyl (C28) sterols predominated, were relatively unaffected by sinefungin. Incorporation of **label** derived from either [methyl-2H3]methionine or [methyl-14C]methionine into sterols was not appreciably affected by treatment at a growth-inhibiting concentration of sinefungin. It was concluded that sinefungin had only a limited effect on sterol production at the 24-transmethylation step, and it is unlikely that this is the primary cause of cell death.
IT **58944-73-3**, Sinefungin
RL: BIOL (Biological study)
(growth and sterol formation by Leishmania response to)
RN 58944-73-3 CAPLUS
CN D-glycero-α-L-talo-Decofuranuronic acid, 6,9-diamino-1-(6-amino-9H-purin-9-yl)-1,5,6,7,8,9-hexadeoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

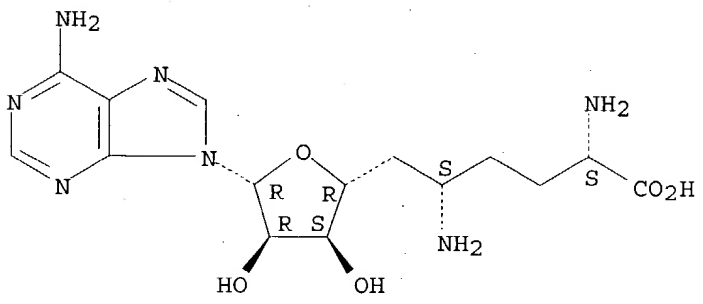


L7 ANSWER 12 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN

09567863

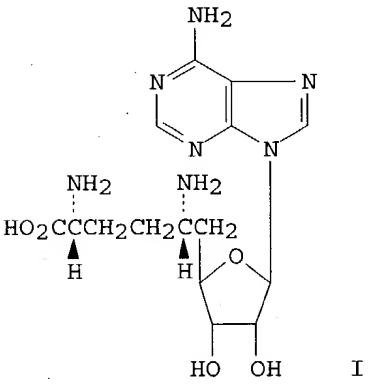
AN 1992:566511 CAPLUS
DN 117:166511
TI Human kidney thiopurine methyltransferase. Photoaffinity **labeling** with S-adenosyl-L-methionine
AU Van Loon, Jon A.; Szumlanski, Carol L.; Weinshilboum, Richard M.
CS Dep. Pharmacol., Mayo Clin./Mayo Found., Rochester, MN, 55905, USA
SO Biochemical Pharmacology (1992), 44(4), 775-85
CODEN: BCPCA6; ISSN: 0006-2952
DT Journal
LA English
AB Thiopurine methyltransferase (TPMT) catalyzes the S-methylation of heterocyclic and aromatic sulfhydryl compds. such as the thiopurine drug 6-mercaptopurine (6-MP). TPMT activity in human tissue is regulated by a common genetic polymorphism, and pharmacogenetic variation in TPMT activity is an important factor in individual differences in thiopurine drug metabolism, toxicity and therapeutic efficacy. Human renal tissue contains two isoenzymes of TPMT, Peak I and Peak II, that can be separated by ion-exchange chromatog. Expts. were performed to determine whether S-adenosyl-L-methionine (Ado-Met), the Me donor for the TPMT reaction, could be used as a photoaffinity ligand for these isoenzymes as one step in the study of the mol. basis for the TPMT genetic polymorphism. When [3H-methyl]Ado-Met and partially purified prepns. of either isoenzyme of human kidney TPMT were exposed to UV light at 254 nm, followed by SDS-PAGE, a 35-kDa protein was the predominant species that was radioactively **labeled**. The same 35-kDa protein was photoaffinity **labeled** with [14C-carboxyl]Ado-Met, demonstrating that **labeling** involved covalent binding of Ado-Met rather than methylation of the protein. TPMT enzymic activity co-eluted with the 35-kDa protein during sequential DEAE ion-exchange, gel filtration and hydroxylapatite chromatog. Inhibitors of TPMT enzymic activity including S-adenosyl-L-homocysteine, sinefungin, 6-methylmercaptopurine and 3,4-dimethoxy-5-hydroxybenzoic acid inhibited photoaffinity **labeling** of the 35-kDa protein in prepns. of both TPMT Peaks I and II isoenzymes in a concentration-dependent fashion, as did 6-MP, the Me acceptor substrate for the TPMT reaction. All of these results were compatible with the conclusion that the 35-kDa protein is TPMT. Photoaffinity **labeling** of TPMT with [3H]Ado-Met should make it possible to purify the enzyme to homogeneity and to study amino acid sequences at or near its active site.
IT **58944-73-3**, Sinefungin
RL: BIOL (Biological study)
(thiopurine methyltransferase isoenzymes of human kidney photoaffinity **labeling** inhibition by)
RN 58944-73-3 CAPLUS
CN D-glycero-α-L-talo-Decofuranuronic acid, 6,9-diamino-1-(6-amino-9H-purin-9-yl)-1,5,6,7,8,9-hexadeoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



09567863

L7 ANSWER 13 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1991:651825 CAPLUS
DN 115:251825
TI The biosynthesis of sinefungin: investigations using a cell-free system
AU Parry, Ronald J.; Ju, Shychen
CS Dep. Chem., Rice Univ., Houston, TX, 77251, USA
SO Tetrahedron (1991), 47(31), 6069-78
CODEN: TETRAB; ISSN: 0040-4020
DT Journal
LA English
GI



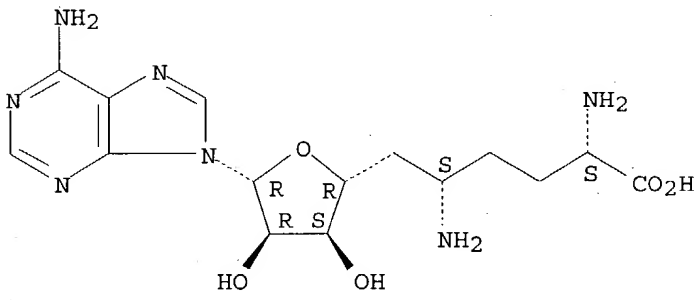
I

AB The origin of the adenylyl moiety of sinefungin (I) was investigated by administration of doubly-**labeled** forms of ATP and adenosine to cell-free exts. of Streptomyces griseolus. Both ATP and adenosine are significantly degraded by the extract before incorporation into I. However, the ribose ring of adenosine was incorporated into I intact, and without loss of 3H from C-5'. This observation rules out the intermediacy of A9145C in I biosynthesis. Addnl. expts. are described which suggest that C-C bond formation between C-5 of arginine and C-5 of a ribose derivative may precede attachment of the adenine ring.

IT **58944-73-3**, Sinefungin
RL: FORM (Formation, nonpreparative)
(formation of, by Streptomyces griseolus, pathway of)

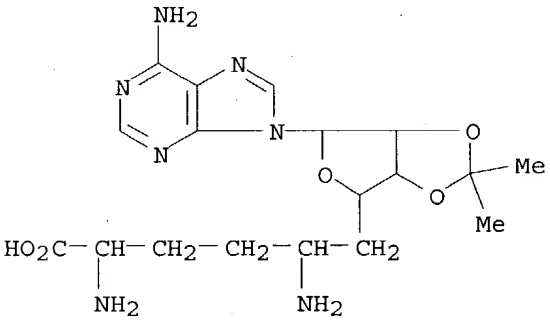
RN 58944-73-3 CAPLUS
CN D-glycero-α-L-talo-Decofuranuronic acid, 6,9-diamino-1-(6-amino-9H-purin-9-yl)-1,5,6,7,8,9-hexadeoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



09567863

IT **137390-83-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 137390-83-1 CAPLUS
CN D-glycero-α-L-talo-Decofuranuronic acid, 6,9-diamino-1-(6-amino-9H-purin-9-yl)-1,5,6,7,8,9-hexadeoxy-2,3-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

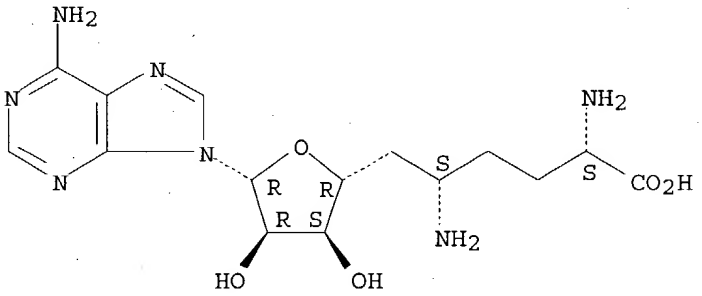


L7 ANSWER 14 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1992:51013 CAPLUS
DN 116:51013
TI Effects of methylthiodeoxyadenosine and its analogs on in vitro invasion of rat ascites hepatoma cells and methylation of their phospholipids
AU Kido, Junichi; Ashida, Yoshiyuki; Shinkai, Kiyoko; Akedo, Hitoshi; Isoai, Atsushi; Kumagai, Hiromichi; Inoue, Hideo
CS Sch. Dent., Univ. Tokushima, Tokushima, 770, Japan
SO Japanese Journal of Cancer Research (1991), 82(10), 1104-11
CODEN: JJCREP; ISSN: 0910-5050
DT Journal
LA English
AB The relationship between tumor invasiveness in vitro and methylation of plasma membrane phospholipids was investigated. For this purpose, 2 hepatoma cell lines, C1-30 and LC-AH, were used which show specific penetration to below cultured monolayers of mesothelial cells from rat mesentery and endothelial cells from calf pulmonary artery, resp. Methylthiodeoxyadenosine (MTA) and 5 of its analogs, difluoro-MTA, deoxyadenosine, sinefungin, phenylthiodeoxyadenosine and fluorophenylthiodeoxyadenosine, inhibited the invasion of the tumor cells without affecting their proliferation. This inhibition was associated with reduction in the incorporation of radioactivity of [methyl-3H]methionine into cellular phosphatidylethanolamine derivs. without changes in the **labelings** of RNA and DNA and carboxymethylation of protein. These compds. also decreased the membrane fluidity of the tumor cells, measured by a steady-state fluorescence polarization method. Three other MTA analogs (fluorodideoxyadenosine, fluoroazidodideoxyadenosine and fluoroaminodideoxyuridine) did not affect the invasiveness of the tumor cells or alter their phospholipid methylation or membrane fluidity at concns. that did not inhibit proliferation. These results suggest that the decrease in inveasiveness of tumor cells by MTA and its analogs is due to alterations in the phospholipid composition and fluidity of the tumor cell membranes.
IT **58944-73-3**
RL: BIOL (Biological study)
(metastasis inhibition by, membrane phospholipid methylation in relation to)
RN 58944-73-3 CAPLUS

09567863

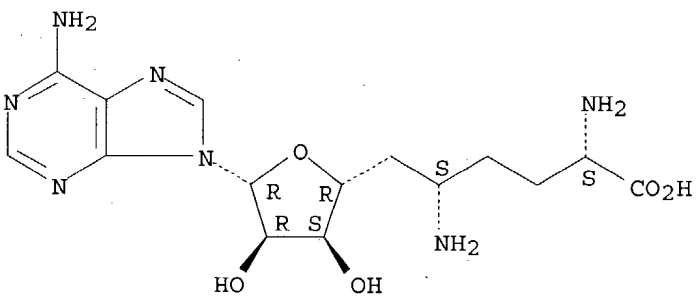
CN D-glycero-α-L-talo-Decofuranuronic acid, 6,9-diamino-1-(6-amino-9H-purin-9-yl)-1,5,6,7,8,9-hexadeoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



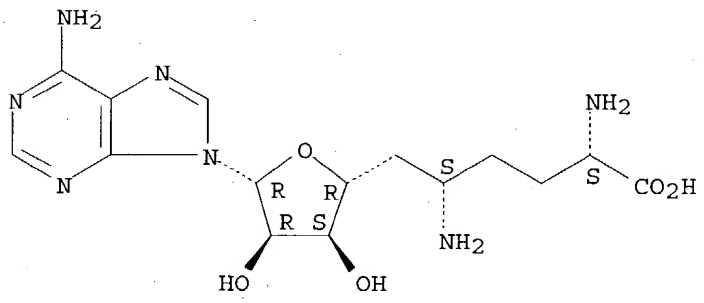
L7 ANSWER 15 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1989:628729 CAPLUS
DN 111:228729
TI Biosynthesis of sinefungin: on the mode of incorporation of L-ornithine
AU Parry, Ronald J.; Arzu, Isidora Y.; Ju, Shyhchen; Baker, Bill J.
CS Dep. Chem., Rice Univ., Houston, TX, 77251, USA
SO Journal of the American Chemical Society (1989), 111(24), 8981-2
CODEN: JACSAT; ISSN: 0002-7863
DT Journal
LA English
AB Investigations of the mechanism of biosynthesis of the nucleoside antibiotic sinefungin are reported. Administration of specifically **labeled** forms of L-ornithine to the producing organism, Streptomyces griseolus, has shown that ornithine is a specific precursor of the antibiotic and that the amino group at C-6' of sinefungin is derived from the δ-amino group of ornithine. Addnl. expts. using (5R)- and (5S)-[5-3H]-L-ornithine revealed that the formation of sinefungin from ornithine proceeds with loss of the 5 pro-S H of the amino acid. C-C bond formation between C-5 of ornithine and C-5' of an adenylyl moiety therefore takes place with overall inversion of configuration at C-5. This stereochem. outcome is unusual, since sinefungin biosynthesis requires pyridoxal phosphate as a cofactor and most enzymic reactions involving this cofactor proceed with overall retention of configuration.
IT **58944-73-3**, Sinefungin
RL: FORM (Formation, nonpreparative)
(formation of, from ornithine by Streptomyces griseolus)
RN 58944-73-3 CAPLUS
CN D-glycero-α-L-talo-Decofuranuronic acid, 6,9-diamino-1-(6-amino-9H-purin-9-yl)-1,5,6,7,8,9-hexadeoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L7 ANSWER 16 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1990:135028 CAPLUS
DN 112:135028
TI The specificity of interaction between S-adenosyl-L-methionine and a nucleolar 2'-O-methyltransferase
AU Segal, David M.; Eichler, Duane C.
CS Coll. Med., Univ. South Florida, Tampa, FL, 33612, USA
SO Archives of Biochemistry and Biophysics (1989), 275(2), 334-63
CODEN: ABBIA4; ISSN: 0003-9861
DT Journal
LA English
AB The structural features of S-adenosyl-L-methionine (SAM) required for optimal binding to a nucleolar RNA 2'-O-methyltransferase were elucidated using various analogs of SAM with modifications of the amino acid, sugar, sulfonium center, and base portions of the mol. Equilibrium binding consts. for SAM and each analog were determined by a nitrocellulose filter binding assay. To ensure the chiral and chemical purity of the 3H-**labeled** SAM used in the binding expts., a cation-exchange HPLC procedure was developed to sep. degradation products of SAM such as adenine and 5'-deoxy-5'-methylthioadenosine, as well as to sep. the (S,S)-SAM from the biol. inactive (R,S)-SAM stereoisomer. S-Adenosyl-L-homocysteine, a product of the methyltransferase reaction, bound equally as well as (S,S)-SAM, indicating that neither the charge nor the Me group at the sulfonium center of (S,S)-SAM is essential for maximal binding. Other modifications of the sulfonium center demonstrated that an S to C atom replacement had little effect on binding affinity, whereas substituting an Et group for the Me group greatly reduced the binding affinity. In addition, the chirality at the sulfonium center was important. The naturally occurring S-chiral form had a 10-fold higher binding affinity than the R-chiral form. No significant stereospecificity was observed relative to the chiral α-C of the methionine moiety in SAM. The α-amino group of methionine and the 6-amino group of adenine were both required for maximal binding, whereas the loss of the 2'-hydroxyl group on the ribose moiety was not. Taken together, these results defined some of the specific geometric and functional group requirements which affect the specificity of interaction between S-adenosyl-L-methionine and the nucleolar 2'-O-methyltransferase.
IT **58944-73-3**, Sinefungin
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with RNA methyltransferase of nucleolus, stereochem. of)
RN 58944-73-3 CAPLUS
CN D-glycero-α-L-talo-Decofuranuronic acid, 6,9-diamino-1-(6-amino-9H-purin-9-yl)-1,5,6,7,8,9-hexadeoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



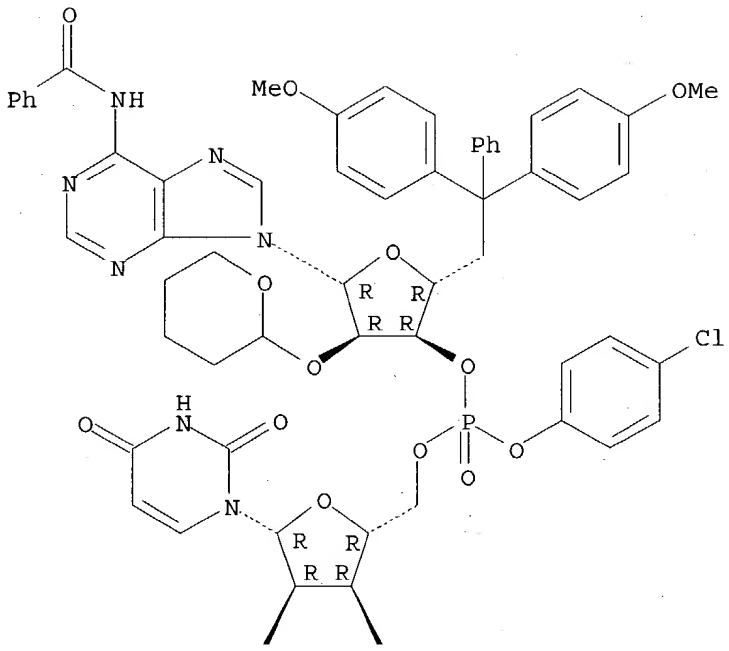
L7 ANSWER 17 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN

09567863

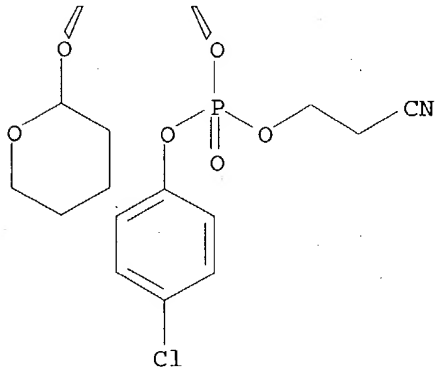
AN 1988:469146 CAPLUS
DN 109:69146
TI Affinity **labeling** of the Escherichia coli ribosomes with the 2',3'-O-[4-(N-2-chloroethyl)-N-methylamino]-benzylidene derivative of AUGU3 within 70S initiation complexes
AU Ven'yaminova, A. G.; Vladimirov, S. N.; Dryga, S. A.; Zenkova, M. A.; Karpova, G. G.; Yamkovoi, V. I.
CS Inst. Bioorg. Chem., Novosibirsk, USSR
SO Bioorganicheskaya Khimiya (1988), 14(3), 321-32
CODEN: BIKHD7; ISSN: 0132-3423
DT Journal
LA Russian
AB Affinity **labeling** of E. coli ribosomes with the 2',3'-O-[4-(N-(2-chloroethyl)-N-methylamino]benzylidene derivative of AUGU3 (I) was studied within 70 S initiation complex ribosome·[14C]I·fMet-tRNAf-met and binary complex ribosome·[14C]I. Various pathways of the 70 S initiation complex formation resulted in differently **labeled** products. Proteins S5, S7, S9, L1, and L16 were crosslinked with [14C]I within an initiation complex obtained in the presence of initiation factors IF-1, IF-2, and IF-3, whereas only proteins S5 and S7 were crosslinked within the complex obtained with the sole factor IF-2. Proteins S1, S3, L1, and L33 were **labeled** within the initiation complex obtained nonenzymically but only protein S1 within the binary complex. In all complexes formed with use of initiation factors **labeling** of IF-2 factor was invariably observed
IT **115520-02-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction with guanosine derivative)
RN 115520-02-0 CAPLUS
CN 3'-Uridylic acid, N-benzoyl-5-O-[bis(4-methoxyphenyl)phenylmethyl]-P-(4-chlorophenyl)-2'-O-(tetrahydro-2H-pyran-2-yl)adenylyl-(3'→5')-2'-O-(tetrahydro-2H-pyran-2-yl)-, 4-chlorophenyl 2-cyanoethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



L7 ANSWER 18 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1988:2551 CAPLUS
DN 108:2551
TI N-Methyltransferase function of the multifunctional enzyme enniatin synthetase
AU Billich, Andreas; Zocher, Rainer
CS Inst. Biochem. Mol. Biol., Tech. Univ. Berlin, Berlin, 1000, Fed. Rep. Ger.
SO Biochemistry (1987), 26(25), 8417-23
CODEN: BICHAW; ISSN: 0006-2960
DT Journal
LA English
AB The N-methyltransferase component of the multifunctional enzyme enniatin synthetase of Fusarium oxysporum was studied. Similar to other transmethylases, S-adenosyl-L-homocysteine (AdoHcy) and sinefungin were

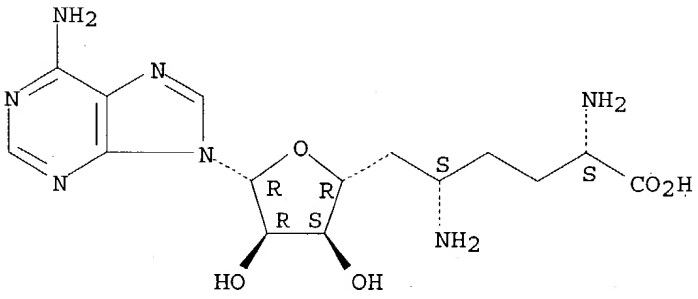
found to be potent inhibitors of the S-adenosyl-L-methionine (AdoMet)-dependent reaction. The Km for AdoMet was 10 μM, and the Ki values for AdoHcy and sinefungin were 4 and 110 μM, resp. Sinefungin acted as a competitive inhibitor with respect to AdoMet, whereas AdoHcy exhibited an inhibition pattern characteristic for a partial competitive inhibitor. This indicated that AdoHcy does not directly compete with AdoMet but binds to a discrete inhibitory site. In addition, AdoHcy inhibited the formation of the unmethylated depsipeptide formed in the absence of AdoMet. In contrast, sinefungin exhibited no influence on the synthesis of demethylenniatin. This finding confirmed the assumption that 2 different binding sites for the inhibitors must be present. Like other methyltransferases, enniatin synthetase could be affinity **labeled** by UV irradiation of the protein in the presence of AdoMet **labeled** at the Me group. The photoreaction was shown to be site specific, and a binding stoichiometry of 1 Me group/enzyme mol. was observed Limited proteolysis of the Me-**labeled** enzyme yielded besides a number of unlabeled fragments only one radiolabeled fragment of mol. weight 25,000, obviously containing the binding site for AdoMet. Evidence was obtained that the binding site for valine, the substrate to be methylated, was not present on this fragment.

IT **58944-73-3**, Sinefungin
RL: BIOL (Biological study)
(amino acid N-methyltransferase component of enniatin synthetase inhibition by, kinetics of)

RN 58944-73-3 CAPLUS

CN D-glycero-α-L-talo-Decofuranuronic acid, 6,9-diamino-1-(6-amino-9H-purin-9-yl)-1,5,6,7,8,9-hexadeoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L7 ANSWER 19 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1987:526631 CAPLUS

DN 107:126631

TI Effect of adenosine analogs on protein carboxylmethyltransferase, S-adenosylhomocysteine hydrolase, and ribonucleotide reductase activity in murine neuroblastoma cells

AU O'Dea, Robert F.; Mirkin, Bernard L.; Hogenkamp, Harry P.; Barten, Donna M.

CS Health Sci. Cent., Univ. Minnesota, Minneapolis, MN, 55455, USA

SO Cancer Research (1987), 47(14), 3656-61
CODEN: CNREA8; ISSN: 0008-5472

DT Journal

LA English

AB The enzymic sites at which adenosine dialdehyde (AD) and other nucleoside analogs exert their cytotoxic effects have been postulated to include protein carboxylmethyltransferase (PCM), S-adenosylhomocysteine (AdoHcy) hydrolase, and ribonucleotide reductase. AD (10-5M) increased PCM activity 350% in suspensions prepared from disrupted cells after 72 h of

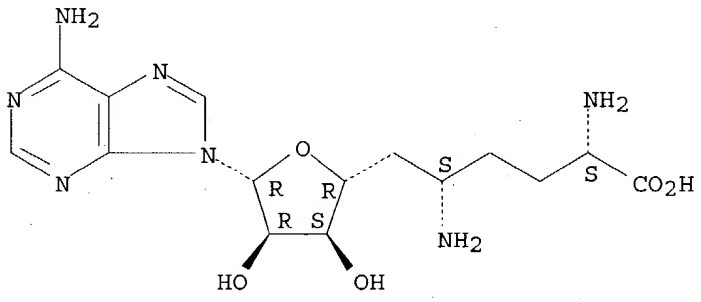
drug exposure; in contrast, 3-deazaadenosine (10-4M) increased PCM activity 57%, whereas AdoHcy and sinefungin had no effect. When intact MNB cells were incubated with AD for varying time periods up to 72 h and then pulse **labeled** with the S-adenosylmethionine precursor L-[3H]-methionine, AD (10-8-5 + 10-6M) produced a concentration-dependent inhibition of protein carboxymethylation which persisted for up to 6 h. Following extended periods of AD treatment (48-72 h), AD (10-6-10-5M) produced a 250% increment in protein carboxymethylation, similar in magnitude to that observed in disrupted cell prepns. This increase in carboxymethylation was observed at times when AdoHcy hydrolase activity remained suppressed. The inhibitory effect of AD on AdoHcy hydrolase activity was maximal within 4 h and still apparent after 72 h of incubation. In contrast, AD treatment had no effect on the ribonucleotide reductase activity of MNB cells. Apparently, the cytotoxic effect of AD on MNB cells results directly from its inhibition of AdoHcy hydrolase activity and indirectly through its suppression of methyltransferase enzyme systems. The potential linkage between the observed long-term elevations in PCM activity and AD-induced cytotoxicity remains to be defined.

IT **58944-73-3**, Sinefungin
RL: BIOL (Biological study)
(protein carboxymethyltransferase inhibition by, cytotoxicity in relation to)

RN 58944-73-3 CAPLUS

CN D-glycero-α-L-talo-Decofuranuronic acid, 6,9-diamino-1-(6-amino-9H-purin-9-yl)-1,5,6,7,8,9-hexadeoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L7 ANSWER 20 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1988:18966 CAPLUS

DN 108:18966

TI Biosynthesis of sinefungin by Streptomyces incarnatus NRRL 8089

AU Malina, H.; Tempete, C.; Robert-Gero, M.

CS Inst Chim. Subst. Nat., Gif-sur-Yvette, 91190, Fr.

SO Symposia Biologica Hungarica (1986), 32(Biol., Biochem. Biomed. Aspects Actinomycetes, Pt. A), 259-61
CODEN: SYBHAK; ISSN: 0082-0695

DT Journal

LA English

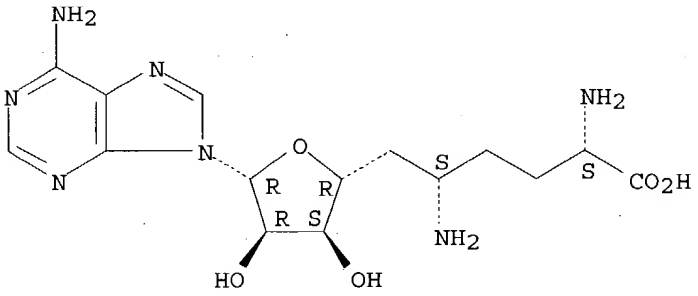
AB Sinefungin was formed from arginine and ATP by S. incarnatus. The product was **labeled** when [U-14C]arginine was a precursor, but not when guanido-**labeled** arginine was used. A reaction mechanism for sinefungin formation, involving activation of an -NH2 of the guanido group to a Schiff base, is proposed.

IT **58944-73-3**, Sinefungin
RL: FORM (Formation, nonpreparative)
(formation of, by Streptomyces incarnatus, pathway of)

09567863

RN 58944-73-3 CAPLUS
CN D-glycero-α-L-talo-Decofuranuronic acid, 6,9-diamino-1-(6-amino-9H-purin-9-yl)-1,5,6,7,8,9-hexadeoxy- (9CI) (CA INDEX NAME)

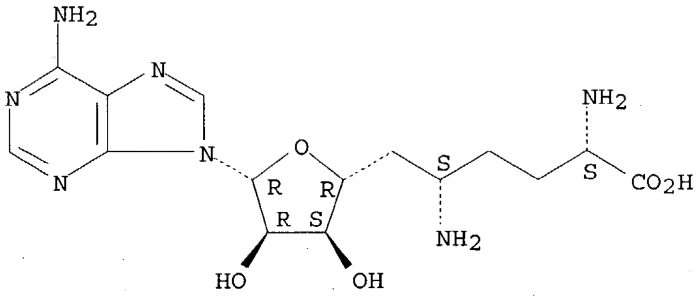
Absolute stereochemistry. Rotation (+).



L7 ANSWER 21 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1985:418886 CAPLUS
DN 103:18886
TI Two histone H1-specific protein-lysine N-methyltransferases from Euglena gracilis. Purification and characterization
AU Tuck, Martin T.; Farooqui, Jamal Z.; Paik, Woon Ki
CS Sch. Med., Temple Univ., Philadelphia, PA, 19140, USA
SO Journal of Biological Chemistry (1985), 260(11), 7114-21
CODEN: JBCHA3; ISSN: 0021-9258
DT Journal
LA English
AB Two forms of a histone H1-specific protein (lysine) N-methyltransferase (protein methylase III) were purified from E. gracilis 48- and 214-fold, resp., with yields of 3.4 and 4.6%. The enzymes were purified on DEAE-cellulose and histone-Sepharose affinity chromatog. and were highly specific toward histone H1 as a substrate. However, 1 of the enzymes also methylated other histone subfractions to a limited extent. Of the proteins other than histones, only myosin showed measurable Me-accepting capability. Both enzymes were inhibited by S-adenosylhomocysteine (D and L forms), S-adenosyl-L-ethionine, and sinefungin, whereas the Ki values for S-adenosyl-L-ethionine were similar for both enzymes, the values for S-adenosyl-L-homocysteine and sinefungin were 10-fold lower for the 2nd form. The Km values for histone H1 and S-adenosyl-L-methionine were 3.1 + 10-7 and 2.7 + 10-5M, resp., for the 1st enzyme, and 4.4 + 10-7 and 3.45 + 10-5M for the 2nd. Peptide anal. of methyl-14C-**labeled** H1 revealed that the 2 enzymes methylate different sites within the histone H1 mol. The 2 enzymes had mol. wts. of 55,000 and 34,000, resp. Both enzymes had an optimum pH of 9.0, which was identical to that of other protein (lysine) N-methyltransferases thus far identified.
IT **58944-73-3**
RL: BIOL (Biological study)
(protein (lysine) methyltransferase of Euglena gracilis inhibition by, kinetics of)
RN 58944-73-3 CAPLUS
CN D-glycero-α-L-talo-Decofuranuronic acid, 6,9-diamino-1-(6-amino-9H-purin-9-yl)-1,5,6,7,8,9-hexadeoxy- (9CI) (CA INDEX NAME)

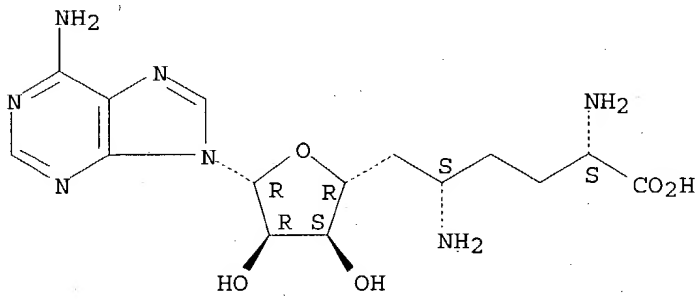
Absolute stereochemistry. Rotation (+).

09567863



L7 ANSWER 22 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1985:451119 CAPLUS
DN 103:51119
TI Effects of Sinefungin on rRNA production and methylation in the yeast Saccharomyces cerevisiae
AU Li, Audrey W.; Singer, Richard A.; Johnston, Gerald C.
CS Dep. Biochem., Dalhousie Univ., Halifax, NS, B3H 4H7, Can.
SO Archives of Biochemistry and Biophysics (1985), 240(2), 613-20
CODEN: ABBIA4; ISSN: 0003-9861
DT Journal
LA English
AB The antifungal agent Sinefungin (SF) is an inhibitor of transmethylation reactions. The effects of SF on the production and methylation of rRNA in S. cerevisiae were examined Under conditions of SF treatment affecting proliferation by this yeast, pulse-chase **labeling** using [methyl-3H]methionine and [3H]uracil indicated that Me incorporation into rRNA during a short **labeling** period was inhibited, and stable 18 S rRNA production was differentially decreased. Other expts. quantitating modified nucleotides in newly produced rRNA showed that stable mols. were methylated. Taken together, these results suggest that SF slows methylation of rRNA, and is associated with differential loss of undermethylated 18 S rRNA species.
IT **58944-73-3**
RL: BIOL (Biological study)
(rRNA formation and methylation inhibition by, in Saccharomyces cerevisiae)
RN 58944-73-3 CAPLUS
CN D-glycero-α-L-talo-Decofuranuronic acid, 6,9-diamino-1-(6-amino-9H-purin-9-yl)-1,5,6,7,8,9-hexadeoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

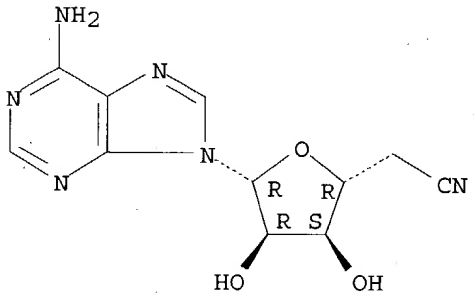


L7 ANSWER 23 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1985:467293 CAPLUS

09567863

DN 103:67293
TI Inactivation of S-adenosylhomocysteine hydrolase by nucleosides
AU Kim, I. Y.; Zhang, C. Y.; Cantoni, Giulio L.; Montgomery, John A.; Chiang, Peter K.
CS Lab. Gen. Comp. Biochem., Natl. Inst. Ment. Health, Bethesda, MD, USA
SO Biochimica et Biophysica Acta (1985), 829(2), 150-5
CODEN: BBACAQ; ISSN: 0006-3002
DT Journal
LA English
AB The irreversible inactivation of S-adenosylhomocysteine hydrolase (I) purified from hamster and bovine liver by adenosine analogs substituted in the 5'- and 2-positions was investigated in detail. 5'-Cyano-5'-deoxyadenosine inactivated as potently as 9-β-D-arabinofuranosyladenine (Ara-A). Substitution of Ara-A at the 2-position by halogens or deleting N at the 3-position decreased its potency. Although weak, 2',3'-dideoxyadenosine could also inactivate I. The irreversible inactivation of I in rat hepatocytes incubated with 2-chloroadenosine or 3-deaza-Ara-A could be demonstrated, concomitant with increases in 35S-**labeled** S-adenosylhomocysteine and S-adenosylmethionine in the hepatocytes.
IT **59696-82-1**
RL: BIOL (Biological study)
(adenosylhomocysteine hydrolase of liver inactivation by, kinetics of, structure-activity relations in)
RN 59696-82-1 CAPLUS
CN β-D-ribo-Hexofuranurononitrile, 1-(6-amino-9H-purin-9-yl)-1,5-dideoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L7 ANSWER 24 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1980:582515 CAPLUS
DN 93:182515
TI Methylation of chemotaxis-specific proteins in Escherichia coli cells permeable to S-adenosylmethionine
AU Rollins, Chiquita M.; Dahlquist, F. W.
CS Inst. Mol. Biol., Univ. Oregon, Eugene, OR, 97403, USA
SO Biochemistry (1980), 19(20), 4627-32
CODEN: BICHAW; ISSN: 0006-2960
DT Journal
LA English
AB By EGTA treatment, E. coli cells were made permeable to S-adenosylmethionine and related mols. to facilitate the study of methylation in chemotaxis. The permeable cells are nonmotile but respond to chemotactic proteins (MCP I and MCP II) in a manner similar to that of untreated, motile cells. Addition of S-adenosyl-L-[methyl-3H]methionine to the permeable cells specifically **labels** 2 proteins, MCP I and MCP II. Methylation of these MCPs depends on the presence of wild-type

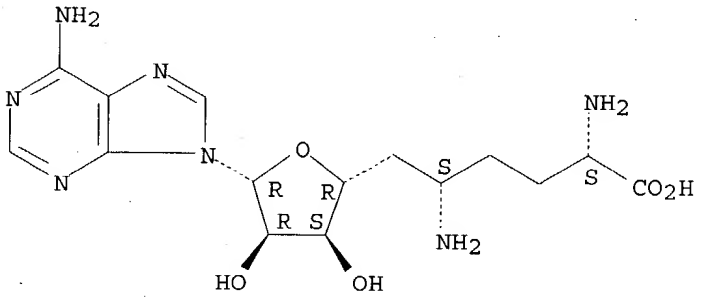
gene products of flaI, flaA, cheB, cheX, tsr, and tar. The extent of methylation of the MCPs is affected by the presence of attractants or repellents. Addition of attractant increases the steady-state level of methylation; addition of repellent causes rapid demethylation to a new steady-state level. Methylation is inhibited by addition of the transmethylase inhibitors A9145C and Sinefungin, which are S-adenosylmethionine analogs, and by S-adenosylhomocysteine.

IT **58944-73-3**
RL: BIOL (Biological study)
(protein methylation in Escherichia coli inhibition by, chemotaxis inhibition in relation to)

RN 58944-73-3 CAPLUS

CN D-glycero-α-L-talo-Decofuranuronic acid, 6,9-diamino-1-(6-amino-9H-purin-9-yl)-1,5,6,7,8,9-hexadeoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L7 ANSWER 25 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1979:4377 CAPLUS

DN 90:4377

TI Incorporation of carbon-14-**labeled** compounds into sinefungin (A9145), a nucleoside antifungal antibiotic

AU Berry, Dennis R.; Abbott, Bernard J.

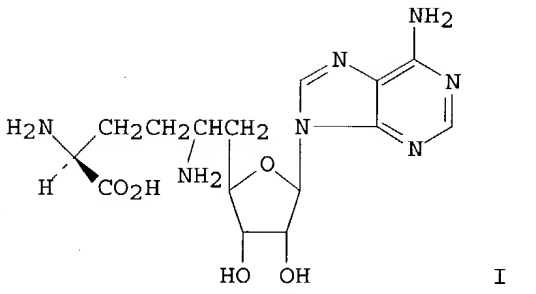
CS Lilly Res. Lab., Eli Lilly and Co., Indianapolis, IN, USA

SO Journal of Antibiotics (1978), 31(3), 185-91
CODEN: JANTAJ; ISSN: 0021-8820

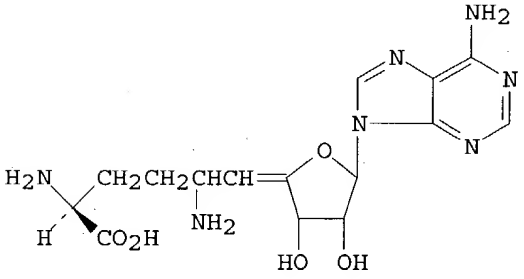
DT Journal

LA English

GI



I



II

AB Streptomyces griseolus produces a complex of antifungal nucleoside antibiotics that contain an ornithine residue linked to the ribose moiety of adenosine. 14C-**labeled** compds. were added to cultures of S. griseolus and the amount of **label** incorporated into the 2-major antifungal components (sinefungin(I) and factor C(II) was measured. Substantial incorporation (16 .apprx. 50%) was obtained with **labeled** adenosine [58-61-7], ATP [56-65-5], adenine [73-24-5], L-ornithine [70-26-8], and DL-citrulline [627-77-0]. Glycine [56-40-6], glucose [50-99-7], L-arginine [74-79-3], and acetate [64-19-7] were incorporated to the extent of 1.7 .apprx. 4.7%. Studies were conducted on the fermentation time course and on the time dependence of **label** incorporation in order to optimize the incorporation of **labeled** adenine into sinefungin. Adenine-8-14C incorporation and sinefungin specific activity were highest 48 h after **label** addition and both declined during subsequent incubation. As much as 43% of the **labeled** adenine was incorporated into the antibiotic and sinefungin was produced with a specific activity of 24.8 μCi/mg. The **labeling** expts. suggest that a preformed adenine derivative (e.g., an adenine nucleotide) and ornithine (or a closely related metabolite) are direct biosynthetic precursors of sinefungin.

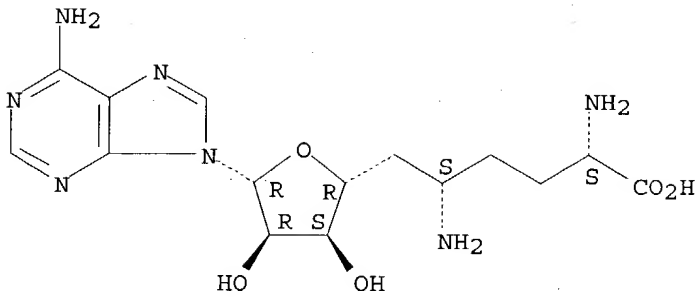
IT **58944-73-3**
RL: FORM (Formation, nonpreparative)
(formation of, by Streptomyces griseolus, precursors of)

RN 58944-73-3 CAPLUS

CN D-glycero-α-L-talo-Decofuranuronic acid, 6,9-diamino-1-(6-amino-9H-purin-9-yl)-1,5,6,7,8,9-hexadeoxy- (9CI) (CA INDEX NAME)

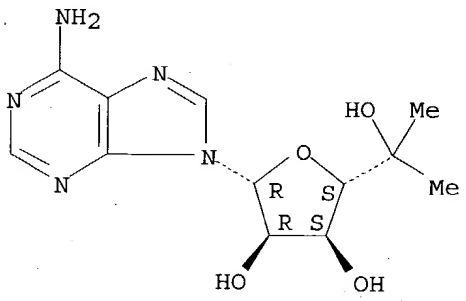
Absolute stereochemistry. Rotation (+).

09567863



L7 ANSWER 26 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1970:404136 CAPLUS
DN 73:4136
TI Mass spectrometry of nucleic acid components. Analogs of adenosine
AU Shaw, Stanley James; Desiderio, Dominic M.; Tsuboyama, Kaoru; McCloskey, James A.
CS Inst. for Lipid Res., Baylor Coll. of Med., Houston, TX, USA
SO Journal of the American Chemical Society (1970), 92(8), 2510-22
CODEN: JACSAT; ISSN: 0002-7863
DT Journal
LA English
AB The mass spectra of adenosine and 32 of its analogs were studied in detail. Principal fragmentation pathways for structurally significant ions were determined and decomposition mechanisms postulated, based on metastable transitions, deuterium and substituent **labels**, and high-resolution mass spectra. The major ions M -30, base +44, and base +30 are proposed to arise from initial transfer of sugar hydroxyl hydrogens to the charge-localized purine base. Methylation at N6 is characterized by elimination of MeN6 with rearrangement of either H or a Me group as previously reported for the corresponding bases. 2'-O-Methylation leads to a unique sugar fragment resulting from elimination of the base plus a 3'- or 5'-hydroxyl H. Anomers are readily distinguished by their mass spectra, but steric orientation of sugar hydroxyls cannot be determined directly. However the abundance of the M - 30 ion was found to depend strongly on the steric accessibility of C-5' to the base.
IT **16046-09-6 22415-88-9**
RL: PRP (Properties)
(mass spectrum of)
RN 16046-09-6 CAPLUS
CN Adenosine, 5',5'-di-C-methyl- (8CI, 9CI) (CA INDEX NAME)

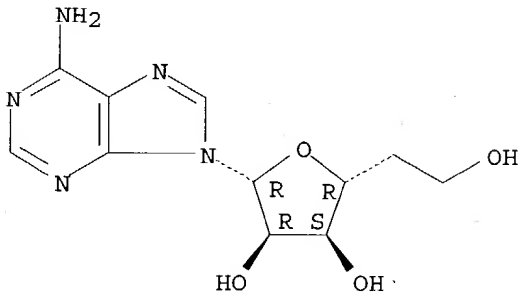
Absolute stereochemistry.



09567863

RN 22415-88-9 CAPLUS
CN 9H-Purin-6-amine, 9-(5-deoxy-β-D-ribo-hexofuranosyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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